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REMARKS

Claims 2, 4, and 27 are canceled. Applicants reserve the right to pursue the canceled subject matter in one or more continuing applications. Claims 1, 3, and 5-26 are pending.

Telephonic Interview with Examiner Tung

Applicants would like to thank Examiner Tung for taking the time to conduct a telephonic interview on February 4, 2004. During the interview Applicants' representatives discussed the amendments made in reply to the Office Action of September 10, 2003. Applicants also expressed their desire to move the claims towards allowance, in view of the fact that the application was facing its seventh office action.

Rejections Under 35 U.S.C. §112, First Paragraph, Enablement.

All pending claims stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification. Applicants respectfully traverse this rejection as to all claims.

The Office Action provides no basis, scientific or otherwise, for this rejection. The only statements offered to justify the rejection are the following:

1. "The claim(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Office Action paper, p.2.
2. "Based upon the claim language ...it is unclear how one skilled in the art would be able to determine whether or not each vector only has one single insertion in the host cell and the single insertion in each vector is different from each other. Therefore one of skill in the art is unable to make or use the invention." Office Action paper, pp.2-3 (Quoted claim language omitted).

The current rejection completely ignores the working Examples provided by Applicants in the present specification. Examples 1, 2 and 3 describe the construction of vectors and inserts, the introduction of vectors and inserts into host cells, and the successful homologous recombination of inserts and vectors in the host cells to make a library. Example 3 further describes the analysis of vectors in nine host cells. All nine cells contained a plasmid vector with

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one insert, **and** each insert was distinct from every other insert. See p.25, line 34-p.26, line 2. Thus, Examples 1-3 in the specification describe **a detailed working example** of the claimed methods.

Applicants also attach in the Appendix a post-filing date reference that describes a commercially available embodiment of the present invention, i.e. a cDNA library made as taught by the present specification. The post-filing date reference is a CLONTECHniques trade publication describing a linearized vector with two ends that are homologous to the two ends of each member of a collection of cDNA inserts. Inserts and vectors are transformed into yeast, thereby generating a complete cDNA library with a "complex collection of distinct clones." P.2, right hand column, (emphasis added); see also figures 1, 3, and 4. This reference provides independent verification, that the present invention can be both made and used by persons of skill in the art.

These two working examples demonstrate that the Office Action is simply incorrect when it asserts that "one of skill in the art is unable to make or use the invention." Both the inventors and others have, in fact, practiced the invention.

Applicants further submit that the language of the current rejection is not clearly directed to any currently claimed element. The Office Action states "it is unclear how one skilled in the art would be able to determine whether or not each vector only has one single insertion in the host cell and the single insertion in each vector is different from each other." None of the rejected claims, however, includes the step of determining whether or not each vector has only one insertion, and that each insertion is different from the other. Therefore, the relevance of the rejection to the pending claims is unclear.

Applicants also point out that the rejection language just quoted is simply incorrect as a statement of fact. Both the specification and the post-filing date reference of Appendix A provide methods of determining whether each vector has one insert and whether each insert is different from every other insert. Example 3 in the specification and Figure 4 of the CLONTECHniques reference both disclose PCR amplification of insert DNA, followed by

restriction enzyme analysis of PCR product. This technique can be used to determine both the number of inserts in a vector and can distinguish between different inserts, therefore in most cases this simple two-step method will be enough to determine whether each vector in a plurality contains only one insert that is different from every other insert in the same plurality. Furthermore, Example 3 in the specification also discloses the DNA sequencing of individual inserts. See p.25, line 34-p.26, line 2. DNA sequencing can be used to unambiguously determine whether or not each vector in a plurality contains only one insert, and whether each insert is different from the other inserts within the plurality.

Thus, contrary to the present rejection, art-recognized molecular biological methods readily lend themselves to the task of determining whether vectors in a plurality contain one, and only one insert, and whether each insert is distinct from every other insert. The Examiner presents no reasons for doubting that skilled artisans would have known these and other methods of making this determination at the time of filing.

Applicants respectfully submit that the even if the current rejection were not factually incorrect, the Examiner's conclusory statements do not establish a *prima facie* basis for an enablement rejection.

> As a matter of Patent Office practice, ... a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented <u>must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein</u> which must be relied on for enabling support. In re Marzocchi, 169 U.S.P.Q. 367, 369 (CCPA 1971) (emphasis added); *citing* In re Gazave, 154 USPQ 92 (1967) and In re Chilowsky, 108 USPQ 321 (1956)

The present Office Action fails to provide **any** reason for doubting the objective truth of the enabling teachings in Applicant's disclosure.

The statement, without any supporting basis, that it is "unclear" how a person of skill in the art would practice the claimed invention appears to misconstrue the burdens of proof in establishing that a disclosure satisfies the enablement requirement of 35 U.S.C. §112. First, as a practical matter, it is imperative that an Examiner provide specific reasons for rejection a claim

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on the basis of enablement, because without such reasons Applicants cannot know how to respond to the rejection (except to say "we disagree"). Second, it is not an applicant's burden to prove that a submitted disclosure is enabling. An Examiner **must** accept a disclosure as enabling, **unless** there is some reason for doubting the disclosure, in which case:

> "...it is incumbent upon the Patent Office, whenever, a rejection on this basis is made, to explain *why* it doubts truth or accuracy of statement in supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with contested statement; otherwise, there would be no need for applicant to support his presumptively accurate disclosure." In re Marzocchi at 370 (emphasis in original); quoted by MPEP §2164.04.

The Examiner's unsupported statement that is "unclear" how a person of skill would practice the invention does not even begin to explain *why* the Examiner doubts that the present disclosure is enabling.

On the other hand, if the Examiner believes the present specification fails to provide essential information for practicing the invention, then an Examiner to explain this deficiency more precisely, as required by MPEP §2164.04, which states:

> the [E]examiner should specifically identify what information is missing **and** why one of ordinary skill in the art could not supply the information without undue experimentation. References should be supplied if possible to support a *prima facie* case of lack of enablement, but are not always required. However, specific technical reasons are always required." (emphasis added) (citations omitted)

The current Office Action provides no reasons, technical or otherwise, as to why missing information from the disclosure would be essential to practice the invention and why such information would not have been available to a person of ordinary skill.

Furthermore, consideration of all the "Wands factors" indicate that the present disclosure would not have required undue experimentation at the time of filing to generate a DNA library using the claimed methods. The present claims are not overly broad; they cover only methods of using homologous recombination to make a single-insert DNA library, and the nature of the invention is not one that requires undue experimentation to practice. As to the state of the prior art and the level of skill in the art at the time of filing: molecular biology and DNA construct making were both well developed at the time of filing. Additionally the level of predictability in

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molecular biology and construct making was high. The application as filed and knowledge in the field therefore provided ample direction for what little additional experimentation may have been necessary. Finally, in yet another Wands factor completely ignored the present rejection, the present disclosure provides working examples.

For the reasons presented above Applicants respectfully submit that the conclusory statements of the present rejection fail to establish even a *prima case* for the present enablement rejection.

Additionally, Applicants would like to briefly address the possibility that the current rejection is based on a misunderstanding of the claims. The Examiner may be misinterpreting the present claims to require that every vector inserted into a host cell homologously recombine with just one insert. Or the Examiner may be misconstruing the present claims to require that every insert comprised by a vector generated by a person practicing the claimed method be distinct from every other insert comprised by a vector in a host cell.

The present claims, though, only require that a **plurality** of vectors, i.e. **more than one**, recombine with one insert, and that every insert **in that plurality** be different from the other inserts in the plurality. Therefore, the present specification needs only to enable a method in which some vectors, i.e. the vectors of the claimed plurality, recombine with one insert or library element.

Since none of the presently claimed methods requires that every vector inserted into a host cell homologously recombine with only one insert, it is simply irrelevant that the present specification does not teach a method whereby every vector inserted into a host cell should contain one, and only one, insert. The present claims do not even require that every vector placed in a host cell recombine with any insert. To reiterate, the present claims only require that some number (more than one) of the vectors placed in a host cell, i.e. a **plurality** of vectors, recombine with just one insert.

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If the teachings of the current specification generate some vectors with no insert, or more than one insert, this does not means that the application is not enabling: it only means that such vectors are not members of the claimed plurality of vectors.

Furthermore, none of the presently claimed methods requires that every insert that recombines with a vector in a host cell be different from every other insert that recombines with a vector in another host cell. The presently claimed methods only require that there be some number of vectors, i.e. those vectors of the claimed plurality, that comprise a different insert or library element. Clearly the present specification does enable multiple vectors, each with a different insert. See Example 3 of the specification and Figure 4 in the Appendix. Vectors that comprise identical inserts or library encoding elements are simply not vectors in the same plurality of vectors recited in the claims.

In sum, even if the present teachings unavoidably produce some vectors that have no insert, or some vectors with more than one insert, or some vectors with identical inserts, nonetheless, Examiner must realize that the present teachings do enable the construction of multiple vectors, i.e. a plurality of vectors, that comprise only one insert; and within that plurality, each vector comprises an insert that is different from the other inserts in the claimed plurality.

For the reasons presented above, Applicants respectfully request that the present rejection be withdrawn as to all claims, and that the present claims be allowed.
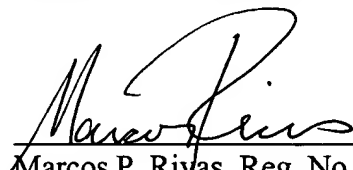
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Respectfully submitted,

Date: May 27, 2004

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